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NEWS
                  "Ask CAS" for self-help around the clock
NEWS
                  EXTEND option available in structure searching
NEWS
       3
          May 12
NEWS
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                  Polymer links for the POLYLINK command completed in REGISTRY
                  New UPM (Update Code Maximum) field for more efficient patent
NEWS
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                  SDIs in CAplus
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NEWS
NEWS
          Jun 28
      7
                  Additional enzyme-catalyzed reactions added to CASREACT
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       8
          Jun 28
                  ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG,
                  and WATER from CSA now available on STN(R)
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          Jul 12
                  BEILSTEIN enhanced with new display and select options,
                  resulting in a closer connection to BABS
NEWS 10
         Jul 30
                  BEILSTEIN on STN workshop to be held August 24 in conjunction
                  with the 228th ACS National Meeting
NEWS 11
         AUG 02
                  IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                  fields
NEWS 12
         AUG 02
                  CAplus and CA patent records enhanced with European and Japan
                  Patent Office Classifications
                  STN User Update to be held August 22 in conjunction with the
NEWS 13
         AUG 02
                  228th ACS National Meeting
NEWS 14
         AUG 02
                  The Analysis Edition of STN Express with Discover!
                  (Version 7.01 for Windows) now available
NEWS 15
         AUG 04
                  Pricing for the Save Answers for SciFinder Wizard within
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NEWS 17 AUG 27 BIOTECHABS/BIOTECHDS: Two new display fields added for legal
status data from INPADOC

NEWS 18 SEP 01 INPADOC: New family current-awareness alert (SDI) available NEWS 19 SEP 01 New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!

NEWS 20 SEP 01 New display format, HITSTR, available in WPIDS/WPINDEX/WPIX NEWS 21 SEP 14 STN Patent Forum to be held October 13, 2004, in Iselin, NJ

NEWS EXPRESS JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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NEWS WWW CAS World Wide Web Site (general information)

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STRUCTURE FILE UPDATES: 20 SEP 2004 HIGHEST RN 748739-98-2 DICTIONARY FILE UPDATES: 20 SEP 2004 HIGHEST RN 748739-98-2

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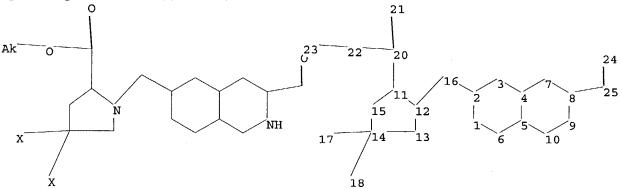
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chain nodes :

16 17 18 20 21 22 23 24 25

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Davis -10/821,698

chain bonds :

2-16 8-25 11-20 12-16 14-17 14-18 20-21 20-22 22-23 24-25

ring bonds :

 $1-2^{-}$ 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-12 11-15 12-13 13-14 14-15

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-12 12-13 12-16 20-21

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containing 1 : 11 :

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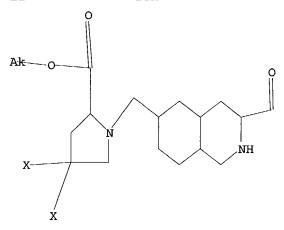
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L1 STRUCTURE UPLOADED

=> dis 11

L1 HAS NO ANSWERS

L1 STF



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=> s l1 sam

SAMPLE SEARCH INITIATED 10:54:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED

1 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 1 TO PROJECTED ANSWERS: 1 TO

1 TO

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L2 1 SEA SSS SAM L1

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100.0% PROCESSED 23 ITERATIONS

5 ANSWERS

SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

=> file caplus

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SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 155.42 155.63

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FILE COVERS 1907 - 21 Sep 2004 VOL 141 ISS 13 FILE LAST UPDATED: 20 Sep 2004 (20040920/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 3 L3

=> s l4 and pd<july 1999 19649264 PD<JULY 1999

(PD<19990700)

L5 0 L4 AND PD<JULY 1999

=> dis l4 1-3 bib abs hitstr

- L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2002:521737 CAPLUS
- DN 137:78867
- TI Preparation of carboxydifluoropyrrolidinylmethyldecahydroisoquinolinecarbo xylates as excitatory amino acid receptor antagonists.
- IN Khau, Vien Van; Letourneau, Michael Edward; Martinelli, Michael John
- PA Eli Lilly and Company, USA
- SO PCT Int. Appl., 54 pp. CODEN: PIXXD2
- DT Patent
- LA English

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PRAI US 2001-260014P
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OS
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$$F = \begin{bmatrix} CO_2R^1 & H & H & H \\ NH & CO_2R^2 & H & H \end{bmatrix}$$

AB Pharmaceutically acceptable salts of title compds. (I; R1, R2 = H, alkyl, alkenyl, alkylaryl, alkylcycloalkyl, alkyldiaminoalkyl, alkylpyrrolidinyl, alkylpiperidinyl, alkylmorpholinyl), were prepared A mixture of Et (3S, 4aR, 6S, 8aR) -6-(hydroxymethyl) -2-(methoxycarbonyl) -1,2,3,4,4a,5,6,7,8,8a-decahydroisoquinoline-3-carboxylate and Et3N in EtOAc is added dropwise to p-nitrobenzenesulfonyl chloride in EtOAc at 0-2° followed by warming to room temperature and stirring for 2.5 h to give 97% sulfonate ester. This was refluxed with hydroxyproline Et ester in EtOAc to give an oil, which in CH2Cl2 was added to a -10° mixture of POC13 and Me2SO in CH2Cl2 to give 41% ketopyrrolidinylmethyldecahydrois oquinoline derivative This was stirred 21 h with deoxofluor [[bis-(2-methoxyethyl)amino]sulfur trifluoride] and EtOH in 1,2-dichloroethane to give 61% difluoropyrrolidinylmethyldecahydroisoquino line derivative, which was N-deprotected with Me3SiI in CH2Cl2 followed by salification with D-mandelic acid to give Et (3S,4aR,6S,8aR)-6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoropyrrolidinyl]methyl]-1,2,3,4,4a,5,6,7,8,8adecahydroisoquinoline-3-carboxylate D-(-)-mandelic acid salt. The dihydrochloride salt of the latter inhibited elec. stimulated dural protein extravasation with ID100 = 0.01 ng/kg orally in rats. 317844-37-4P 440632-08-6P 440632-09-7P TT

I

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

Davis -10/821,698

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of carboxydifluoropyrrolidinylmethyldecahydroisoquinolinecarbox ylates as excitatory amino acid receptor antagonists)

RN 317844-37-4 CAPLUS

CN

3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1-pyrrolidinyl]methyl]decahydro-, ethyl ester, dihydrochloride, (3S,4aR,6S,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

•2 HCl

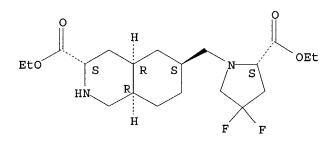
RN 440632-08-6 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1-pyrrolidinyl]methyl]decahydro-, ethyl ester, (3S,4aR,6S,8aR)-, mono[(αR)-α-hydroxybenzeneacetate] (9CI) (CA INDEX NAME)

CM 1

CRN 317844-31-8 CMF C20 H32 F2 N2 O4

Absolute stereochemistry.



CM 2

CRN 611-71-2 CMF C8 H8 O3

Absolute stereochemistry. Rotation (-).

RN 440632-09-7 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1-pyrrolidinyl]methyl]decahydro-, ethyl ester, (3S,4aR,6S,8aR)-, 1,5-naphthalenedisulfonate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 317844-31-8 CMF C20 H32 F2 N2 O4

Absolute stereochemistry.

CM 2

CRN 81-04-9 CMF C10 H8 O6 S2

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:521727 CAPLUS

DN 137:78866

TI Preparation of pyrrolidinyl- and piperidinylmethyldecahydroisoquinolinecar boxylates as excitatory amino acid receptor antagonists.

IN Filla, Sandra Ann; Hudziak, Kevin John; Mathes, Brian Michael; Ornstein, Paul Leslie

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 116 pp. CODEN: PIXXD2

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DT
     Patent
LA
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     PATENT NO.
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PRAI US 2001-259921P
                          Ρ
     WO 2001-US44714
                          W
                                20011220
os
     MARPAT 137:78866
GΙ
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Title compds. e.g., [I; R1 = H, Cl, Br, iodo, F, SR3, OH; R2 = H, F; R3 = (substituted) tetrazolyl, triazolyl, alkyl, carboxyalkyl; with provisos], were prepared for treatment of e.g., migraine and pain (no data). Thus, Et (3S,4aR,6S,8aR)-6-hydroxymethyl-2-methoxycarbonyldecahydroisoquinoline-3-carboxylate was tosylated followed by coupling with trans-4-OH-L-proline Et ester hydrochloride. The product was oxidized with Me2SO/(COCl)2 in CH2Cl2 followed by fluorination of the resulting ketone with DAST and deprotection with Me3SiCl to give Et (3S,4aR,6S,8aR)-6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoropyrrolidinyl]methyl]-1,2,3,4,4a,5,6,7,8,8a-decahydroisoquinoline-3-carboxylate.

IT 317844-31-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidinyl- and piperidinylmethyldecahydroisoquinolinecarb oxylates as excitatory amino acid receptor antagonists)

RN 317844-31-8 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1-pyrrolidinyl]methyl]decahydro-, ethyl ester, (3S,4aR,6S,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
L4
ΝA
    2001:31316 CAPLUS
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DN 134:91148

Selective iGluR5 receptor antagonists for the treatment of migraine TI

IN Bleakman, David; Chappell, Amy Suzon; Filla, Sandra Ann; Johnson, Kirk Willis; Ornstein, Paul Leslie

PA Eli Lilly and Company, USA

PCT Int. Appl., 34 pp. SO

CODEN: PIXXD2

DT Patent

English LA

FAN.CNT 1

	PATENT NO.			APPLICATION NO.	
ΡI	WO 2001001972	A2	20010111	WO 2000-US16297	
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AΒ The present invention provides a method of treating or preventing migraine which comprises administering to a patient in need thereof an effective amount of a selective iGluR5 receptor antagonist. The present invention further provides novel compds. functional as selective iGluR5 receptor antagonists, i.e., isoquinoline carboxylate derivs., as well as compns.

Davis -10/821,698

and formulations comprising said selective iGluR5 receptor antagonists. Formulations of hard gelatin capsules, tablets, an aerosol solution, suppositories, suspensions, and i.v. injections are provided. For example, i.v. administration of 3S,4aR,6S,8aR-6-(((4-carboxy)phenyl)methyl)-1,2,3,4,4a,5,6,7,8,8a-decahydroisoquinoline-3-carboxylic acid (preparation given) inhibited dural protein extravasation, a functional characteristic of migraine, with ID50 of 6.5 and 4.0 ng/kg in rats and guinea pigs, resp.

IT 317844-31-8P 317844-35-2P 317844-37-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of selective iGluR receptor antagonists for treatment of migraine)

RN 317844-31-8 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1pyrrolidinyl]methyl]decahydro-, ethyl ester, (3S,4aR,6S,8aR)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

RN 317844-35-2 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1-pyrrolidinyl]methyl]decahydro-, ethyl ester, (3S,4aR,6S,8aR)-, mono(α -hydroxybenzeneacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 317844-31-8 CMF C20 H32 F2 N2 O4

Absolute stereochemistry.

CM 2

CRN 90-64-2 CMF C8 H8 O3

RN 317844-37-4 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 6-[[(2S)-2-(ethoxycarbonyl)-4,4-difluoro-1-pyrrolidinyl]methyl]decahydro-, ethyl ester, dihydrochloride, (3S,4aR,6S,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

●2 HCl

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